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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,185	02/25/2002	Thomas Dag Horn	023533-0144	4869

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 07/26/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,185	HORN ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *10-12,16-32 and 40-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,13-15 and 33-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Re: Horn *et al.*

Date of priority: 06/25/1999

The Election filed 05/10/04 in response to the Office Action of 04/09/04 is acknowledged and has been entered.

Applicant's election with traverse of Group II, claims 1-9, 13-15, 33-39, and 42-45 is acknowledged. Applicants further select group (d), bacterial and candida antigens. The traversal is on the ground(s) that a search of bacterial antigens in combination with either candida (group e) or trichophyton (group f) antigens would not impose a serious burden, as both antigens are fungal antigens. This is not found persuasive as a search for the broad claims (i.e. Claims 1-7) includes *any* two antigens in the world. Thus, there is a high burden of search criteria. Further, the literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Also, MPEP 802.01 provides that restriction is proper between inventions which are independent or distinct. Here, the inventions of the various groups are distinct for the reasons set forth in the Action mailed 04/09/04. Different searches and issues are involved in the examination of each group. For these reasons the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-47 are pending.

Claims 10-12, 16-32, 40-46 have been withdrawn from further consideration by the examiner under 37 CFR 1.142(b) as being drawn to non-elected inventions.

Claims 1-9, 13-15, and 33-39 are currently under consideration.

Claim Objections

Claims 8-9 are objected to for reciting antigens drawn to non-elected subject matter. Applicants election was drawn to a search and examination of bacterial and candida antigens.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 34-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims recite "wherein said antigens are equivalent in purity to an allergenic extract for intradermal testing" which is indefinite as the specification does not disclose any examples or references points for determining or defining the purity of an allergenic extract. Thus, the metes and bounds of the claims cannot be determined.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-7, 13-15, and 33-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description in this case only sets forth a pharmaceutical composition for treating an epithelial tumor in a subject comprising a bacterial antigen and a candida antigen wherein each of said antigens induces or is capable of inducing a delayed type hypersensitivity response in the subject. Thus, the written description is not commensurate in scope with the claims drawn to a genus of antigens including at least any two antigens in the world.

The specification does not provide a specific limitation to what is included or excluded by "antigens"; only that said antigens induce or be capable of inducing a delayed type hypersensitivity (DTH) response (page 7, para 21). Hence, the antigens comprise a wide genus of any substance that elicits an immune response. A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to the genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cNDA, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., __F.3d__,2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of antigens that encompass the genus of antigens that may be capable of inducing DTH nor does it provide a description of structural features that are common to the antigens. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure(s) of the encompassed genus of antigens, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only a pharmaceutical composition for treating an epithelial tumor in a subject comprising a bacterial antigen and a candida antigen wherein each of said antigens induces or is capable of inducing a delayed type hypersensitivity response in the subject, but not the full breadth of the claims, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Claims 1-9, 13-15, and 33-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a pharmaceutical composition for treating a *benign* epithelial tumor, does not reasonably provide enablement for a pharmaceutical composition capable of treating any type of epithelial tumor including cervical carcinomas or melanomas (Claim 5). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the

predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The specification discloses that the invention includes the treatment of both benign and malignant epithelial tumors (page 8, para 24). However, there is insufficient guidance and objective evidence that such compositions would predictably treat any malignant epithelial tumor. In fact, the claims are broadly inclusive of a cancer vaccine. However, the specification only supports the immunotherapy or resolution of benign epithelial tumors, i.e. warts (Table B, page 16). Those of skill in the art of oncology recognize that the immunotherapeutic treatment of established carcinomas is highly unpredictable. For example, Bellone *et al.* (Immunology Today, v20 (10), 1999, pp.457-462) summarize the state of the art of peptide immunotherapy including clinical trials where "there is usually a poor correlation between induction of specific T-cells and the clinical responses" (page 457, 2nd column). Bellone *et al.* teach the disadvantages of peptide cancer immunotherapy in that (1) there is no direct evidence for a role in tumor rejection, (2) the therapy is applicable to few patients, (3) risk of generating tumor escape mutants, and (4) risk of autoimmune reactions (page 461, Box 1). Indeed, Gaiger *et al.* (Blood, Volume 96, No. 4, August 2000, pages 1480-1489) chose to evaluate the Wilm's tumor antigen (WT1) as a potential immunotherapeutic as it is well known in the art that WT1 protein expression is more abundant in leukemia cells than in normal hematopoietic ells. However, WT1 peptide immunization did not show any effect on tumor growth in-vivo (Figure 10, page 1486). All of this underscores the criticality of providing workable examples which is not disclosed in the specification, particularly in an unpredictable art, such as cancer therapy.

In view of the teachings above, and the lack of guidance and or exemplification in the specification, it would not be predictable for of skill in the art to use the pharmaceutical compositions as broadly contemplated in the disclosure. Thus, it would require undue experimentation by one of skill in the art to practice the invention as broadly claimed.

Claim Rejections - 35 USC § 102

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-9, 13-14, 33-36, and 38 are rejected under 35 U.S.C. 102(e) as being anticipated by Clements, J. (US Patent No. 6,033,673, March 18, 1998).

Clements teaches a pharmaceutical composition comprising at least two antigens and a pharmaceutically acceptable carrier, wherein said antigens are selected from the group consisting of bacterial and *candida albicans* antigens (column 9, line 43; column 10, line 28; column 12, line 14). Clements further teaches (column 9, line 9) that the compositions include the promotion of cell-mediated responses which encompasses antigens that induce or are capable of inducing DTH. Clements further teaches wherein said subject is a human mammal (column 10, line 5). Although the reference does not characterize the antigens as useful for treating an epithelial tumor, such a characterization is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the product *per se*, a pharmaceutical composition comprising at least two antigens and a pharmaceutically acceptable carrier. Further, due to the indefiniteness of the claim language as set forth above, it is

assumed for examination purposes that said antigens are equivalent in purity to an allergenic extract for intradermal testing.

Claims 1-9, 13-14, 33-36, 38 are further rejected under 35 U.S.C. 102(e) as being anticipated by Bostwick, E. (US2002/0009429 A1, January 29, 1999).

Bostwick, E. teaches a pharmaceutical composition comprising at least two antigens and a pharmaceutically acceptable carrier, wherein said antigens are selected from the group consisting of bacterial and *candida albicans* antigens (see page 8, column 2, under claims). Clements further teaches administration of the pharmaceutical compositions to animals including humans (para 20). Although the reference does not characterize the antigens as useful for treating an epithelial tumor, such a characterization is merely suggestive of an intended use and is not given weight for purposes of comparing the claims with the prior art. The claims read on the product *per se*, a pharmaceutical composition comprising at least two antigens and a pharmaceutically acceptable carrier. Further, due to the indefiniteness of the claim language as set forth above, it is assumed for examination purposes that said antigens are equivalent in purity to an allergenic extract for intradermal testing.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 13-15, and 33-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bostwick, E. (US2002/0009429 A1, January 29, 1999) or Clements, J. (US Patent No. 6,033,673, March 18, 1998) in further view of the CANDIN® package insert text, IDS, Reference A12, submitted March 14, 2003.

Both Clements and Bostwick teach as set forth above with regards to claims 1-9, 13-15, 33-36, and 38.

Neither reference specifically teaches a kit comprising a hypodermic needle or a high pressure injection device comprising the pharmaceutical composition of Claim 1 (Claim 15) or wherein the *Candida albicans* extract for intradermal testing is the *Candida albicans* Skin Test Antigen (Claims 37 and 39).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include kits comprising injections devices such as hypodermic needles

comprising the pharmaceutical compositions as taught by both Clements and Bostwick. On one hand, Clements already suggests the desirability of packaging the compositions into kit form (column 9, line 65+). On the other hand, both references teach that the pharmaceutical compositions may be administered intramuscsularly or subcutaneously (Clements- column 9, line 48; Bostwick, para 30). Hence, it would be obvious to anyone of ordinary skill to include an injection device comprising the pharmaceutical antigens for the purposes of inoculation. Further, kits provide for increased marketability, convenience, reliability, and economy. Further, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to include the *Candida albicans* Skin Test Antigen. Both references suggest and encourage the use of *Candida albicans* antigens in their pharmaceutical compositions and according to the the CANDIN® package insert, the Skin Test Antigen is readily available and easily assessable.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 571-272-0835. The examiner can normally be reached on M-Th, 8:30-5:30; alternate Fri., 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gary B. Nickol Ph.D.
Primary Examiner
Art Unit 1642

GBN
July 13, 2004

GARY B. NICKOL, PH.D.
PRIMARY EXAMINER